REMARKS

In the Office Action dated July 1, 2009, claims 1-17 and 22-71 were rejected. The Examiner made the rejection final. In response, Applicant has filed an RCE and in the present response has not amended any of the clams, but submits the following comments. Reconsideration of this application is requested in view of the following remarks.

In the Office Action, claims 1-17 and 22-71 stand rejected under the judicially-created doctrine of obviousness type double patenting as being unpatentable over the claims of U.S. Patent Nos. 5,843,928; 6,114,317; 6,392,071; 6,440,953; 6,482,812; 6,537,981; 6,566,352; 6,579,861; 6,627,622; 6,696,431; 6,774,251; 6,806,262; 6,887,860; 6,894,037; 6,992,074; 7,053,075; 7,094,774; 7,115,594; 7,141,558; 7,208,484; 7,214,670; 7,214,671; 7,232,810; 7,241,747; 7,241,748; 7,241,909; 7,244,719; 7,300,925 and 7,511,030 in view of Bishop et al U.S. 5,972,917 or DeLuca et al WO 96/16035. The Examiner contends that each of these patents teaches 2-alkylidene-19-nor vitamin D compounds useful in treating various diseases such as osteoporosis. Although the Examiner recognizes that the instantly claimed compounds differ from the 2-alkylidene-19-nor vitamin D compounds of the prior art as being 18, 19-dinor derivatives thereof, the Examiner believes that said compounds are obvious over the cited patents. Applicant disagrees that the presently-claimed compounds are rendered obvious in view of the cited patents for the following reasons.

In the Office action, the Examiner states:

> "The Examiner maintains that the comparison made by applicant is not a true side-by side comparison. Although, the data obtained by the references was obtained by the same procedures, it does not follow that it is a true side-by-side comparison. The skilled artisan in the art would know that two laboratories utilizing the same assay can obtain differ [sic] results. Additionally, the workup/preparation is as important as the assay utilized."

The Examiner then proceeds to list several differences between the assays set forth in the present application and those in US 5,843,928 relating to (a) the diet of the animals; (b) the vehicle in which the compound was dissolved; (c) the duration of administration; and (d) the handling of the blood obtained for the assay, in support of her position. Applicant would like to address the Examiner's statement that the previous comparisons were not "true" side-by-side comparisons by referring the Examiner to the enclosed DeLuca Declaration. The DeLuca Declaration addresses

each of he Examiner's noted differences and concludes that none will affect the outcome of the data, and each is insignificant to obtaining consistent results.

Under the present circumstances, although the data referred to by Applicant is found in a number of different prior art references, all of the data was obtained by the same procedures, and was obtained via the same techniques. The differences noted by the Examiner are insignificant, as evidenced by the DeLuca Declaration. As such, the data would be considered by those skilled in the art to be true comparative data. Although the data was obtained at different times and locations, the data was obtained via the same techniques, and is thus a true comparison of the biological activities of all of these compounds.

In the Office Action, the Examiner also states:

> "Based on said teachings and the knowledge in the art of 18,19-dinor vitamin D compounds, the skilled artisan would have the reasonable expectation that the 18,19-dinor derivatives of the cited patents would show selective activity on calcium mobilization."

By the following argument, Applicant will demonstrate to the Examiner that the biological activities of 18,19-dinor-vitamin D compounds are unpredictable, and thus one skilled in the art will not be able to predict with any certainty the activity of any particular 18,19-dinor vitamin D compound until such vitamin D compound is actually tested for such activities. As such, one skilled in the art could not predict with any reasonable expectation of success that a particular 18,19-dinor compound would be useful to treat a disease such as osteoporosis, or would show selective activity on calcium mobilization, as the Examiner alleges.

In order to demonstrate to the Examiner that the activity of the corresponding 18-nor vitamin D analog is unpredictable as compared to the structurally similar 19-nor parent compound having a methyl group at the 18 position, Applicant will hereinafter compare the biological activities of two different groups of vitamin D compounds. The first comparison is between 19-nor-1α,25-dihydroxyvitamin D_3 versus 18,19-dinor-1α,25-dihydroxyvitamin D_3. The second comparison involves 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol versus 1α-hydroxy-2-methylene-18,19-dinor-homopregnacalciferol.

The biological activities of 19-nor-1α,25-dihydroxyvitamin D_3 versus 18,19-dinor-1α,25-dihydroxyvitamin D_3 are given in WO 96/16035 which is cited by the Examiner in the present

Office Action. The calcemic activity of these compounds is given in Table 1 at page 27 thereof. WO 96/16035 concludes that:

> "Table 1 shows that 18,19-dinor-1α,25-dihydroxyvitamin D_3, while having similar ability to mobilize calcium from bone, is clearly not as active in this regard as 1α,25-dihydroxyvitamin D_3. Also, Table 1 shows that 18,19-dinor-1α,25-dihydroxyvitamin D_3 is almost as active as 1α,25-dihydroxyvitamin D_3 in intestinal calcium transport activity.
>
> Thus, the 18,19-dinor analog shows a selective activity profile combining high potency in inducing the differentiation of malignant cells, relatively high intestinal calcium transport activity with relatively low bone calcium mobilization activity. The compounds of this novel structural class, therefore, can be useful as therapeutic agents for the treatment of psoriasis and other malignancies, and for the treatment of metabolic bone diseases where bone loss is a major concern such as osteoporosis, osteomalacia and renal osteodystrophy."

Thus, WO 96/16035 concludes that the 18,19-dinor analog taught therein may be useful to treat osteoporosis, even though it has different calcemic activities than the corresponding parent analog 19-nor-1α,25-dihydroxyvitamin D_3. Again, however, it is opined that the 18,19-dinor compound may be useful to treat metabolic bone diseases depending upon the relevant medical facts of a patient's condition even though it has "relatively low" bone calcium mobilization activity.

The Examiner cites U.S. 6,440,953 as an example of a 2-methylene-19-nor compound in which the corresponding 18-nor compound would be expected to show selective activity on calcium mobilization. However, the data published in connection with the corresponding 18-nor analog thereof demonstrates otherwise. More specifically, Applicant refers the Examiner to U.S. Patent No. 7,238,681 which teaches the corresponding 18,19-dinor analog of the 2-methylene-19-nor analog disclosed in U.S. 6,440,953 cited by the Examiner. The biological activity of the 18,19-dinor compound disclosed in '681 is set forth in Figures 4 and 5, and discussed at column 13, line 53 through column 14, line 2 as follows:

> "FIG. 4 shows that 18,19-dinor-2MP has little, if any, activity in mobilizing calcium from bone, and its activity is about equivalent to 2MP. Administration of 18,19-dinor-2MP at 780 pmol/day for 4 consecutive days did not result in mobilization of bone calcium, and increasing the amount of 18,19-dinor-2MP to 2340 pmol/day or to 7020 pmol/day was also without any substantial effect.

> Intestinal calcium transport was evaluated in the same groups of animals using the everted gut sac method (FIG. 5). These results show that the compound 18,19-dinor-2MP does not promote intestinal calcium transport when administered at 780 pmol/day, 2340 pmol/day or 7020 pmol/day, whereas $1,25(OH)_2D_3$ promotes a significant increase at the 780 pmol/day dose, and 2MP also provides a significant increase at a 2340 pmol/day dose. Thus, it may be concluded that 18,19-dinor-2MP is essentially devoid of intestinal calcium transport activity at the tested doses."

As the Examiner can see, the corresponding 18,19-dinor compound has little, if any, calcemic activity. As a result, this compound does not have selective activity on bone calcium mobilization, as the Examiner predicts. The Examiner will specifically note that in the '681 patent no mention is made of this compound's usefulness in treating metabolic bone diseases. The obvious reason is that it has no calcemic activity.

Thus, the 18,19-dinor compound disclosed in U.S. 7,238,681, although being an 18,19-dinor compound, would not show selective activity on bone calcium mobilization and thus would not be useful in treating metabolic bone diseases. If, as alleged by the Examiner, one skilled in the art would have a reasonable assumption that the 18,19-dinor analog disclosed in the '681 reference would have selective activity on bone calcium mobilization and thus would have been useful to treat metabolic bone diseases, that person skilled in the art would be wrong.

In summary, one skilled in the art cannot predict the biological activities of corresponding 18,19-dinor compounds. As such, one skilled in the art would not have a reasonable expectation of success in predicting the biological activities of 18,19-dinor analogs, as alleged by the Examiner. Withdrawal of the obviousness type double patenting rejection based on Bishop et al '917 and/or DeLuca et al '035 is herein requested.

In the Office Action, claims 1-17 and 22-71 were also provisionally rejected on the ground of non-statutory obviousness type double patenting as being unpatentable over the claims of co-pending application nos. 10/997,698; 11/697,414; 11/697,434 and 11/697,436 in view of Bishop et al '917 or DeLuca et al '035.

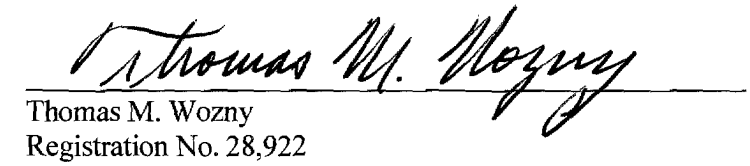
In response, Applicant states that it believes it has addressed the non-provisional obviousness type double patenting rejections based upon the prior art patents via the present response, and as a result traverses the present rejection for the same reasons as noted above. Thus, if the Examiner agrees with those arguments, and withdraws the double patenting rejections based upon the issued patents cited previously herein, with the result that this

provisional obviousness type double patenting rejection is the only remaining rejection, then Applicant requests the Examiner withdraw this provisional rejection so that the present application may proceed to issuance. Reconsideration and withdrawal of this provisional rejection is therefore requested.

An effort has been made to place this application in condition for allowance and such action is earnestly requested.

Respectfully submitted,

ANDRUS, SCEALES, STARKE & SAWALL, LLP



Thomas M. Wozny
Registration No. 28,922

Andrus, Sceales, Starke & Sawall, LLP
100 East Wisconsin Avenue, Suite 1100
Milwaukee, Wisconsin 53202
Telephone: (414) 271-7590
Facsimile: (414) 271-5770